	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	49678	diabetes	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/07 14:47			0
2	BRS	L2	3785	type adj ii adj diabetes	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/07 14:47			0
3	BRS	L3	209	lxr	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/07 14:49			0
4	BRS	L4	51	liver adj x adj receptor	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/07 14:49			0
5	BRS	L5	49	(3 or 4) same agonist	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/07 14:50			0
6	BRS	L6	2	(1 or 2) same 5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/07 14:53			0
7	BRS	L7	6979	hyperglycemia or (insulin adj resistance) or (plasma adj glucose adj level)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/07 14:55			0
8	BRS	L8	1	5 same 7	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/07 14:55			0
9	BRS	L9	2434	thiazolidinedione or cigitazone or pioglitazone or troglitazone or rosiglitazone	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/07 14:56			0
10	BRS	L10	6	5 same 9	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/07 14:56			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
11	BRS	L11	0	10 same 1	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/07 14:56			0

FILE 'MEDLINE' ENTERED AT 15:00:1[redacted]N 07 JUL 2003

FILE 'CAPLUS' ENTERED AT 15:00:11 ON 07 JUL 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 15:00:11 ON 07 JUL 2003
COPYRIGHT (C) 2003 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'EMBASE' ENTERED AT 15:00:11 ON 07 JUL 2003
COPYRIGHT (C) 2003 Elsevier Science B.V. All rights reserved.

FILE 'SCISEARCH' ENTERED AT 15:00:11 ON 07 JUL 2003
COPYRIGHT 2003 THOMSON ISI

FILE 'AGRICOLA' ENTERED AT 15:00:11 ON 07 JUL 2003

=> s diabetes
L1 697215 DIABETES

=> s type II diabetes
L2 13387 TYPE II DIABETES

=> s lxr or (liver x receptor)
L3 1454 LXR OR (LIVER X RECEPTOR)

=> s l3 (p) agonist
L4 307 L3 (P) AGONIST

=> s (l1 or l2) (p) l4
L5 21 (L1 OR L2) (P) L4

=> duplicate remove l5
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L5
L6 6 DUPLICATE REMOVE L5 (15 DUPLICATES REMOVED)

=> d l6 1-6 ibib abs

L6 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:300597 CAPLUS
DOCUMENT NUMBER: 138:314591
TITLE: Methods for affecting various diseases utilizing LXR compounds
INVENTOR(S): Schulman, Ira G.; Bischoff, Eric D.; Tangirala, Rajendra K.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 33 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003073614	A1	20030417	US 2001-982544	20011017

PRIORITY APPLN. INFO.: US 2001-982544 20011017

AB The invention relates to methods for elevating high d. lipoprotein (HDL) plasma levels, decreasing the absorption of dietary cholesterol in the intestine, decreasing the plasma level of low d. lipoprotein (LDL), and increasing the conversion of cholesterol to bile acids, utilizing ***LXR*** .beta. selective ***agonists*** , usually without elevating the plasma levels of triglycerides. Also provided are methods of using such ***agonists*** to treat metabolic diseases alone or in combination with other active agents. Also provided are methods for decreasing hyperglycemia and insulin resistance methods for treating ***type*** ***II*** ***diabetes*** , and methods for treating ***type*** ***II*** ***diabetes*** and reducing the cardiovascular complications of ***type*** ***II*** ***diabetes*** , utilizing an ***LXR*** ***agonist*** . Further provided are methods for treating obesity and methods for treating the complications of obesity including ***type*** ***II*** ***diabetes*** , cardiovascular disease, hyperlipidemia, and

hypertension, administering ***LXR*** .alpha.-selective antagonist.

L6 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:376503 CAPLUS
DOCUMENT NUMBER: 138:362624
TITLE: Assays for liver X receptor (LXR) modulators
INVENTOR(S): Gustafsson, Jan- Ke; Schuster, Gertrud; Nebb, Hilde Irene
PATENT ASSIGNEE(S): Karo Bio AB, Swed.
SOURCE: Brit. UK Pat. Appl., 36 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2381866	A1	20030514	GB 2001-27132	20011112

PRIORITY APPLN. INFO.: GB 2001-27132 20011112

AB Assays for identifying agents for the treatment of ***diabetes*** or disorders of fatty acid or cholesterol metab., by identifying modulators (ligands, ***agonists*** or antagonists) that bind to or modulate the biol. activity of ***liver*** ***X*** ***receptor*** alpha or beta (***LXR*** .alpha. or ***LXR*** .beta.). Such modulators may alter the amt. of at least one of SREBP-1, cholesterol 7.alpha.-hydroxylase (Cyp7A), fatty acid synthetase, human cholesterol ester transfer protein (CETP), ***LXR*** .alpha. or ***LXR*** .beta. protein or mRNA levels. The assay may be performed in hepatocyte, adipocyte or preadipocyte cells. The assay may be performed in combination with a retinoid X receptor (RXR). Use of agents identified by such assays in the prepn. of medicaments and methods of treating ***diabetes*** are also claimed.
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 6 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2003007893 MEDLINE
DOCUMENT NUMBER: 22401814 PubMed ID: 12414791
TITLE: Antidiabetic action of a liver x receptor agonist mediated by inhibition of hepatic gluconeogenesis.
AUTHOR: Cao Guoqing; Liang Yu; Broderick Carol L; Oldham Brian A; Beyer Thomas P; Schmidt Robert J; Zhang Youyan; Stayrook Keith R; Suen Chen; Otto Keith A; Miller Anne R; Dai Jiannong; Foxworthy Patricia; Gao Hong; Ryan Timothy P; Jiang Xian-Cheng; Burris Thomas P; Eacho Patrick I; Etgen Garret J
CORPORATE SOURCE: Lilly Research Laboratories, Eli Lilly & Company, Indianapolis, Indiana 46285, USA.. guoqing_cao@lilly.com
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2003 Jan 10) 278 (2) 1131-6.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20030107
Last Updated on STN: 20030308
Entered Medline: 20030307

AB The oxysterol receptors ***LXR*** (***liver*** ***X*** ***receptor***)-alpha and LXRbeta are nuclear receptors that play a key role in regulation of cholesterol and fatty acid metabolism. We found that ***LXRs*** also play a significant role in glucose metabolism. Treatment of diabetic rodents with the ***LXR*** ***agonist*** , T0901317, resulted in dramatic reduction of plasma glucose. In insulin-resistant Zucker (fa/fa) rats, T0901317 significantly improved insulin sensitivity. Activation of ***LXR*** did not induce robust adipogenesis but rather inhibited the expression of several genes involved in hepatic gluconeogenesis, including phosphoenolpyruvate carboxykinase (PEPCK). Hepatic glucose output was dramatically reduced as a result of this regulation. Nuclear run-on studies indicated that transcriptional repression was primarily responsible for the inhibition of PEPCK by the ***LXR*** ***agonist*** . In addition, we show that the regulation of the liver gluconeogenic pathway by ***LXR*** ***agonists*** was a direct effect on hepatocytes. These data not only suggest that ***LXRs*** are novel targets for ***diabetes*** but also reveal an

unanticipated role for these receptors, further linking lipid and glucose metabolism.

L6 ANSWER 4 OF 6 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2002396032 MEDLINE
DOCUMENT NUMBER: 22139932 PubMed ID: 12145154
TITLE: Liver X receptors downregulate 11beta-hydroxysteroid dehydrogenase type 1 expression and activity.
AUTHOR: Stulnig Thomas M; Oppermann Udo; Steffensen Knut R; Schuster Gertrud U; Gustafsson Jan-Ake
CORPORATE SOURCE: Department of Medical Nutrition and Biosciences, Karolinska Institutet, Huddinge, Sweden.. thomas.stulnig@akh-wien.ac.at
SOURCE: DIABETES, (2002 Aug) 51 (8) 2426-33.
Journal code: 0372763. ISSN: 0012-1797.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020730
Last Updated on STN: 20030108
Entered Medline: 20020821

AB 11Beta-hydroxysteroid dehydrogenase type 1 (11beta-HSD-1) converts inactive corticosteroids into biologically active corticosteroids, thereby regulating the local concentration of active glucocorticoids, such as cortisol. 11beta-HSD-1 is particularly expressed in adipocytes and liver and appears to be causally linked to the development of type 2 ***diabetes*** and the metabolic syndrome. ***Liver*** ***X*** ***receptor*** (***LXR***)-alpha and -beta are nuclear oxysterol receptors whose key role in lipid metabolic regulation has recently been established. In this study, we show that treatment of adipocytes derived from 3T3-L1 cells and mouse embryonic fibroblasts in vitro with synthetic or natural ***LXR*** ***agonists*** decreases mRNA expression of 11beta-HSD-1 by approximately 50%, paralleled by a significant decline in 11beta-HSD-1 enzyme activity. Downregulation of 11beta-HSD-1 mRNA by ***LXRs*** started after a lag period of 8 h and required ongoing protein synthesis. Moreover, long-term per os treatment with a synthetic ***LXR*** ***agonist*** downregulated 11beta-HSD-1 mRNA levels by approximately 50% in brown adipose tissue and liver of wild-type but not of LXRalpha(-/-)beta(-/-) mice and was paralleled by downregulation of hepatic PEPCK expression. In conclusion, ***LXR*** ligands could mediate beneficial metabolic effects in insulin resistance syndromes including type 2 ***diabetes*** by interfering with peripheral glucocorticoid activation.

L6 ANSWER 5 OF 6 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2002675571 MEDLINE
DOCUMENT NUMBER: 22323543 PubMed ID: 12435796
TITLE: Novel roles of liver X receptors exposed by gene expression profiling in liver and adipose tissue.
AUTHOR: Stulnig Thomas M; Steffensen Knut R; Gao Hui; Reimers Mark; Dahlman-Wright Karin; Schuster Gertrud U; Gustafsson Jan-Ake
CORPORATE SOURCE: Department of Medical Nutrition and Biosciences, Karolinska Institutet, Huddinge, Sweden.. thomas.stulnig@akh-wien.ac.at
SOURCE: MOLECULAR PHARMACOLOGY, (2002 Dec) 62 (6) 1299-305.
Journal code: 0035623. ISSN: 0026-895X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20021119
Last Updated on STN: 20021227
Entered Medline: 20021209

AB ***Liver*** ***X*** ***receptor*** (***LXR***) alpha and LXRbeta are nuclear oxysterol receptors whose biological function has so far been elucidated only with respect to cholesterol and lipid metabolism. To expose novel biological roles for ***LXRs*** , we performed genome-wide gene expression profiling studies in liver and white and brown adipose tissue from wild-type (LXRalpha(+/+)beta(+/+)) and knockout mice (LXRalpha(-/-)beta(-/-)) treated with a synthetic ***LXR*** ***agonist*** . By an adapted statistical analysis, we detected 319 genes significantly regulated by ***LXR*** ***agonist*** treatment in wild-type but not in knockout mice, fulfilling most stringent criteria

with an overall confidence of 94%. Down-regulation of essential enzymes of gluconeogenesis in liver could point to possible beneficial effects of ***LXR*** ***agonists*** in ***diabetes*** mellitus. ***LXR*** ***agonist*** treatment also altered expression of genes involved in steroid hormone synthesis and growth hormone receptor signaling, emphasizing a potential impact on endocrine function. Notably, ***LXR*** ***agonist*** treatment up-regulated CYP4A10 and CYP4A14 together with cytochrome P450 reductase, indicating a possible enhancement of microsomal lipid peroxidation. In conclusion, these gene expression profiling data identify novel areas of regulation by ***LXRs*** and provide a highly valuable basis for further research on the biological functions of these nuclear receptors and the pharmacological characteristics of their ligands.

L6 ANSWER 6 OF 6 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 97238686 MEDLINE
DOCUMENT NUMBER: 97238686 PubMed ID: 9121558
TITLE: Sensitization of diabetic and obese mice to insulin by retinoid X receptor agonists.
AUTHOR: Mukherjee R; Davies P J; Crombie D L; Bischoff E D; Cesario R M; Jow L; Hamann L G; Boehm M F; Mondon C E; Nadzan A M; Paterniti J R Jr; Heyman R A
CORPORATE SOURCE: Department of Cardiovascular Research, Ligand Pharmaceuticals, San Diego, California 92121, USA.
SOURCE: NATURE, (1997 Mar 27) 386 (6623) 407-10.
Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970506
Last Updated on STN: 20030318
Entered Medline: 19970418

AB Retinoic acid receptors (RAR), thyroid hormone receptors (TR), peroxisome proliferator activated receptors (PPARs) and the orphan receptor, ***LXR*** , bind preferentially to DNA as heterodimers with a common partner, retinoid X receptor (RXR), to regulate transcription. We investigated whether RXR-selective ***agonists*** replicate the activity of ligands for several of these receptors? We demonstrate here that RXR-selective ligands (referred to as rexinoids) function as RXR heterodimer-selective ***agonists*** , activating RXR: PPARgamma and RXR: ***LXR*** dimers but not RXR:RAR or RXR:TR heterodimers. Because PPARgamma is a target for antidiabetic agents, we investigated whether RXR ligands could alter insulin and glucose signalling. In mouse models of noninsulin-dependent ***diabetes*** mellitus (NIDDM) and obesity, RXR ***agonists*** function as insulin sensitizers and can decrease hyperglycaemia, hypertriglyceridaemia and hyperinsulinaemia. This antidiabetic activity can be further enhanced by combination treatment with PPARgamma ***agonists*** , such as thiazolidinediones. These data suggest that the RXR:PPARgamma heterodimer is a single-function complex serving as a molecular target for treatment of insulin resistance. Activation of the RXR:PPARgamma dimer with rexinoids may provide a new and effective treatment for NIDDM.

=> d his

(FILE 'HOME' ENTERED AT 14:59:36 ON 07 JUL 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 15:00:11 ON 07 JUL 2003
L1 697215 S DIABETES
L2 13387 S TYPE II DIABETES
L3 1454 S LXR OR (LIVER X RECEPTOR)
L4 307 S L3 (P) AGONIST
L5 21 S (L1 OR L2) (P) L4
L6 6 DUPLICATE REMOVE L5 (15 DUPLICATES REMOVED)

=> s thiazolidinedione or cigitazone or pioglitazone or troglitazone or rosiglitazone
L7 15998 THIAZOLIDINEDIONE OR CIGITAZONE OR PIOGLITAZONE OR TROGLITAZONE OR ROSIGLITAZONE

=> s l7 (p) l4
L8 12 L7 (P) L4

=> s l8 (p) l1

```
L9           5 L8 (P) L1

=> duplicate remove l9
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L9
L10           1 DUPLICATE REMOVE L9 (4 DUPLICATES REMOVED)

=> d l10 1 ibib abs

L10  ANSWER 1 OF 1     MEDLINE                              DUPLICATE 1
ACCESSION NUMBER:    97238686     MEDLINE
DOCUMENT NUMBER:     97238686   PubMed ID: 9121558
TITLE:               Sensitization of diabetic and obese mice to insulin by
                     retinoid X receptor agonists.
AUTHOR:              Mukherjee R; Davies P J; Crombie D L; Bischoff E D; Cesario
                     R M; Jow L; Hamann L G; Boehm M F; Mondon C E; Nadzan A M;
                     Paterniti J R Jr; Heyman R A
CORPORATE SOURCE:    Department of Cardiovascular Research, Ligand
                     Pharmaceuticals, San Diego, California 92121, USA.
SOURCE:              NATURE, (1997 Mar 27) 386 (6623) 407-10.
                     Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY:        ENGLAND: United Kingdom
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199704
ENTRY DATE:          Entered STN: 19970506
                     Last Updated on STN: 20030318
                     Entered Medline: 19970418
AB   Retinoic acid receptors (RAR), thyroid hormone receptors (TR), peroxisome
     proliferator activated receptors (PPARs) and the orphan receptor,
       ***LXR***  , bind preferentially to DNA as heterodimers with a common
     partner, retinoid X receptor (RXR), to regulate transcription.  We
     investigated whether RXR-selective   ***agonists***   replicate the
     activity of ligands for several of these receptors? We demonstrate here
     that RXR-selective ligands (referred to as rexinoids) function as RXR
     heterodimer-selective   ***agonists***  , activating RXR: PPARgamma and
     RXR:  ***LXR***   dimers but not RXR:RAR or RXR:TR heterodimers.  Because
     PPARgamma is a target for antidiabetic agents, we investigated whether RXR
     ligands could alter insulin and glucose signalling.  In mouse models of
     noninsulin-dependent   ***diabetes***   mellitus (NIDDM) and obesity, RXR
       ***agonists***   function as insulin sensitizers and can decrease
     hyperglycaemia, hypertriglyceridaemia and hyperinsulinaemia.  This
     antidiabetic activity can be further enhanced by combination treatment
     with PPARgamma   ***agonists***  , such as   ***thiazolidinediones***  .
     These data suggest that the RXR:PPARgamma heterodimer is a single-function
     complex serving as a molecular target for treatment of insulin resistance.
     Activation of the RXR:PPARgamma dimer with rexinoids may provide a new and
     effective treatment for NIDDM.


=> d his

     (FILE 'HOME' ENTERED AT 14:59:36 ON 07 JUL 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     15:00:11 ON 07 JUL 2003
L1        697215 S DIABETES
L2         13387 S TYPE II DIABETES
L3          1454 S LXR OR (LIVER X RECEPTOR)
L4           307 S L3 (P) AGONIST
L5            21 S (L1 OR L2 ) (P) L4
L6             6 DUPLICATE REMOVE L5 (15 DUPLICATES REMOVED)
L7         15998 S THIAZOLIDINEDIONE OR CIGITAZONE OR PIOGLITAZONE OR TROGLITAZO
L8            12 S L7 (P) L4
L9             5 S L8 (P) L1
L10            1 DUPLICATE REMOVE L9 (4 DUPLICATES REMOVED)

=> log y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    36.43      36.64

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -1.30      -1.30
```